Transcriptional Regulation of Cardiac Pacemaker Cell Progenitors

Grant Award Details

Transcriptional Regulation of Cardiac Pacemaker Cell Progenitors

Grant Type: New Faculty I

Grant Number: RN1-00562

Project Objective: Goals: to selectively identify progenitor cells destined to become pacemakers or working myocytes and understand the mechanisms of cardiac conduction system specification.

Investigator:

Name:	Mohammad Pashmforoush
Institution:	University of Southern California
Type:	PI

Disease Focus: Heart Disease

Human Stem Cell Use: Embryonic Stem Cell

Award Value: $2,816,578

Status: Closed

Progress Reports

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Reporting Period: Year 4

View Report

Reporting Period: Year 5

View Report

Reporting Period: NCE

View Report

Grant Application Details

Application Title: Transcriptional Regulation of Cardiac Pacemaker Cell Progenitors

Public Abstract: Congenital and acquired defects of cardiac pacemakers are leading causes of morbidity and mortality in our society. Dysfunctions of the SA node and the lower conduction cells lead to a variety of complex arrhythmias that typically necessitate anti-arrhythmic therapy and implantation of devices. These treatments have significant limitations in their efficacy and risk-benefit ratio. Thus, it would be ideal to generate cell-based therapeutic approaches towards treating arrhythmias. Experimental data has provided compelling evidence that pacemaker and conduction cells of the heart separate early in development from the working myocardium and retain a relatively undifferentiated state. Prior cell-based approaches in regenerating myocardial damage in the heart have met limited success in part due to implantation of a diverse population of cells. This generally results in poor engraftment and undesirable outcomes. There is now evidence for resident conduction progenitor cells in myocardium that orchestrate the process of cell recruitment into the conduction tissue. In the current proposal we aim to identify the molecular events that lead to differentiation and formation of cardiac pacemaker cells. We will utilize the information obtained from the above experiments to generate cell based methods to treat cardiac arrhythmias. We aim to genetically manipulate the human embryonic stem cells so we can identify a selected population that is destined to become pacemaker cells. By replacing the cells responsible for normal beating of the heart, we hope to provide natural therapies for human conduction system disease

Statement of Benefit to California: The ultimate of goal of our proposal is identify a reliable mechanism for implementing a cell-based approach for treating human arrhythmias. Sudden cardiac death related to cardiac arrhythmia is a leading cause of morbidity and mortality in our society. The people of California have voted to implement new innovative ways of treating human disease by using human stem cells, the current project is in line with such wishes to create new therapeutic modalities towards treating heart disease.